

*REMARKS/ARGUMENTS*

*The Pending Claims*

Claims 1-5, 7-10, 12, 13, 16-22, and 40 are pending and are directed to a method of inducing an immunological response.

*Amendments to the Claims*

The claims have been amended to point out more particularly and claim more distinctly the invention. In particular, claim 1 has been amended to incorporate the features of claims 6, 11, 14, and 15 (now canceled).

Claim 7 has been amended to recite a feature that previously was recited in claim 1.

Claim 21 has been amended to recite a feature that previously was recited in claim 17.

Claim 40 has been amended to depend from claim 1 and to recite that the one or more DNA segments comprises SEQ ID NO: 1 (the DNA sequence of MUC-1(6)) and SEQ ID NO: 3 (the DNA sequence of CEA(6D)) or encodes SEQ ID NO: 2 (the amino acid sequence of MUC1(6)) and SEQ ID NO: 4 (the amino acid sequence of CEA(6D)).

Claims 6, 11, 14, 15, 25-39, and 41-43 have been canceled. Applicants reserve the right to pursue the canceled subject matter in one or more divisional, continuation, continuation-in-part, or other applications.

No new matter has been added by way of these amendments to the claims.

*Summary of the Office Action*

The Office makes final the restriction requirement and withdraws non-elected claims 23-32 and 41-43 from consideration.

The Office objects to claim 7.

The Office rejects claims 1-14 and 33-40 under 35 U.S.C. § 102(b) as allegedly anticipated by Schliom et al. (WO 00/34494).

The Office rejects claims 1 and 4-16 under 35 U.S.C. § 103(a) as allegedly obvious over Schlam et al. and Pecher (WO 01/24832). The Office rejects claims 1, 6, 7, 11, and 17-22 under 35 U.S.C. § 103(a) as allegedly obvious over Schlam et al. and Grosenbach et al. (*Cancer Res.*, 61: 4497-4505 (2001)).

The Office rejects claims 35-38 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Reconsideration of these objections and rejections is hereby requested.

#### *Discussion of the Claim Objection*

The Office contends that claim 7 is indefinite since it depends from itself. Claim 7 has been amended to depend from claim 1. Applicants believe that the objection is moot in view of the amendment to claim 7.

#### *Discussion of the Anticipation Rejection*

The Office contends that the subject matter of claims 1-14 and 33-40 is anticipated by Schlam et al. This rejection is traversed for the following reasons.

Claim 1 (from which the remaining pending claims depend directly or indirectly) has been amended to incorporate the features of claim 15, which the Office did not include in the anticipation rejection. The pending claims, as amended, now recite that the first and second poxvirus vector comprise mucin (MUC) and carcinoembryonic antigen (CEA), which the Office acknowledges is not taught by Schlam et al.

Accordingly, Applicants request that the anticipation rejection be withdrawn.

#### *Discussion of the Obviousness Rejections*

The Office contends that it would have been obvious to one of ordinary skill in the art to arrive at the methods recited in claims 1 and 4-16 based on the teachings of the Schlam and Pecher references. The Office also contends that it would have been obvious to one of ordinary skill in the art to arrive at the methods recited in claims 1, 6, 7, 11, and 17-22 based

on the teachings of the Schlam and Gosenbach references. The obviousness rejections are traversed for the following reasons.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned *Graham* factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

As regards the scope and content of the prior art, the Office contends that the Schlam reference discloses a prime-boost protocol for the treatment or prevention of cancer, wherein viral vectors, such as poxvirus vectors, encode an antigen. The Office contends that the Pecher reference discloses the combined administration of vectors, including vaccinia virus vectors, encoding MUC-1 and CEA to human patients for treatment of tumors. The Office contends that the Gosenbach reference discloses a vaccine strategy for administering poxvirus encoding CEA and TRICOM, wherein a vaccinia virus encoding CEA and TRICOM is administered followed by three boosts of a fowlpox virus encoding CEA and TRICOM.

For purposes of the analysis here, and for the sake of argument, the level of ordinary skill can be considered to be relatively high, such that a person of ordinary skill in the art would have an advanced degree and/or several years of experience in the relevant field.

The present invention, as defined by the pending claims, is directed to a method for inducing an immunological response against a cell expressing a breast cancer associated antigen in a human, wherein the method comprises selecting a human having breast cancer or

at risk for developing such a breast cancer tumor, administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) MUC or an antigenic portion thereof or modified version thereof and (ii) CEA or an antigenic portion thereof or modified version thereof, and at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) MUC or antigenic portion thereof or modified version thereof and (ii) CEA or an antigenic portion thereof or modified version thereof, such that an immunological response against the cell expressing the breast cancer associated antigen is induced in the individual.

None of the cited references discloses a prime-boost protocol, wherein administration of a first poxvirus vector comprising two tumor-associated antigens (MUC and CEA) is followed by subsequent administrations of a second poxvirus vector comprising two tumor-associated antigens (MUC and CEA) for the induction of an immune response against malignant pancreatic cancer cells, as required by the pending claims.

The Office acknowledges that the Schlom reference does not disclose a poxvirus vector encoding MUC and CEA, let alone a prime-boost protocol employing two poxvirus vectors encoding MUC and CEA, as required by the pending claims.

It appears that the Pecher reference (the portions of the Pecher reference cited to by the Office are not translated into English) discloses a composition comprising a first vector (e.g., a plasmid or vaccinia vector) comprising the gene encoding MUC-1 and a second vector comprising the gene encoding CEA. Thus, MUC and CEA are not in the same vector, as required by the pending claims.

The Office relies on the Grosenbach reference for its disclosure of a prime/boost strategy comprising the administration of a vaccinia virus encoding CEA and TRICOM (i.e., the costimulatory molecules B7-1, ICAM, and LFA-3) followed by a fowlpox virus encoding CEA and TRICOM. The Grosenbach reference does not disclose a vector encoding MUC and CEA, as required by the pending claims.

Thus, the disclosures of the Pecher and Grosenbach references do not remedy the deficiencies of the Schlom reference in that they do not disclose a prime-boost protocol to

treat breast cancer wherein the first and second poxvirus vectors encode both MUC and CEA, as required by the pending claims.

Furthermore, the existence of unexpected benefits attendant the present invention further evidence the nonobviousness of the present invention, as defined by the pending claims, over the combination of the disclosures of the cited references.

The inventors discovered that a prime-boost protocol comprising administration of first poxvirus vector comprising the tumor-associated antigens MUC and CEA followed by subsequent administrations of a second poxvirus vector comprising MUC and CEA resulted in the induction of an immune response against breast cancer cells. The specification describes a Phase I clinical trial, which established the preliminary safety and efficacy profiles of targeted cancer immunotherapy using a prime-boost protocol in cancer patients (see, e.g., paragraphs 258-274). As confirmed by the post-filing Gulley reference (*Clin. Cancer Res.*, 14(10): 3060-3069 (2008)); a copy of which is submitted herewith), a prime-boost protocol comprising administration of a first poxvirus vector comprising the tumor-associated antigens MUC and CEA followed by subsequent administrations of a second poxvirus vector comprising MUC and CEA, as recited in the pending claims, resulted in the development of a significant increase in antigen-specific (MUC or CEA) immune response in patients (see, e.g., Abstract; page 3063, column 1, second paragraph, through page 3064, column 2, second paragraph; and page 3068, column 2, third paragraph) and evidence of clinical benefit (see, e.g., Abstract).

Considering all of the *Graham* factors together, it is clear that the present invention – as defined by the pending claims – would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of the Schlam and Pecher references or the Schlam and Grosenbach references. Accordingly, the obviousness rejections should be withdrawn.

#### *Discussion of the Indefiniteness Rejections*

The Office contends that the metes and bounds of claims 35-38 are unclear due to the recitation of the term “about.” Claims 35-38 have been canceled, thereby rendering moot the indefiniteness rejection of these claims.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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Rachel J. Mejdrich, Reg. No. 53,477  
LEYDIG, VOIT & MAYER, LTD.  
Two Prudential Plaza, Suite 4900  
180 North Stetson Avenue  
Chicago, Illinois 60601-6731  
(312) 616-5600 (telephone)  
(312) 616-5700 (facsimile)

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